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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/506,703

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Michael S. Kopreski

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11/06/2009

MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP
300 S. WACKER DRIVE
32ND FLOOR
CHICAGO, IL 60606

EXAMINER

NATARAJAN, MEERA

ART UNIT

PAPER NUMBER

1643

MAIL DATE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/506,703	Applicant(s) KOPRESKI, MICHAEL S.	
	Examiner MEERA NATARAJAN	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 July 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24, 26 and 28-36 is/are pending in the application.
- 4a) Of the above claim(s) 1-9, 16, 17, 21, 22, 24, 26 and 28-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 10-15, 18-20, 23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>06/04/2009</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's amendments in the reply filed on 07/30/2009 are acknowledged and entered into the record.
2. Accordingly, Claims 1-24, 26, 28-36 are pending. Claims 1-9, 16, 17, 21, 22, 24, 26, 28-36 are withdrawn as being drawn to non-elected inventions.
3. Claims 10-15, 18-20, and 23 will be examined on the merits.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 10-15, 18-20, and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kopreski et al. (Clinical Cancer Research, Vol. 5, 1961-1965, August 1999) in view of Kang et al. (2001 Oct;81(19):1176-9, see Abstract) and Mok et al. (J. Natl. Cancer Inst. Vol. 93(9), pp.1458-1464, Oct, 2001).

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7. The Claims are drawn to method of detecting extracellular RNA from an apoptotic body in pleural effusions from a patient, the method comprising extracting, separating, isolating or purifying the apoptotic body from serum, labeling RNA in the apoptotic body or cDNA derived therefrom or its amplified product using a labeled primer or probe specific to RNA or cDNA derived therefrom and detecting the labeled RNA or cDNA from the apoptotic bodies using fluorescent labeled probes, flow cytometry, or hybridizing the extracted RNA to a solid substrate such as a bioelectric interface.

8. Kopreski et al. teach detecting extracellular RNA in the serum of patients with malignant melanoma and in serum samples from normal volunteers as controls. Kopreski et al. disclose detection of tyrosine mRNA in the samples from patients with malignant melanoma. Kopreski et al. disclose in the "Materials and Methods" the serum was prepared by centrifugation at 830 X g for 10 min. Although Kopreski et al. do not specifically disclose the RNA detected is from apoptotic bodies, the instant specification defines apoptotic bodies "are separated from the cellular fraction of a bodily fluid by centrifugation, wherein the non-cellular centrifuged fraction contains the apoptotic body" (see p. 8, lines 15-17 of the instant specification). Therefore, Kopreski et al. inherently detects RNA from apoptotic bodies by performing the same method for isolating apoptotic bodies as disclosed in the instant specification. Kopreski et al. also disclose in the "Materials and Methods", amplification and detection of the RNA using specific primers and probes and detection methods such as gel electrophoresis and southern blot. Kopreski et al. does not teach isolating apoptotic body RNA from pleural effusions

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or using a bioelectric interface. These deficiencies are made up for by Kang et al. and Mok et al.

9. Kang et al. teach analysis of malignant pleural effusion caused by lung carcinoma before and after therapy. Flow cytometry, optical microscopy, electron microscopy and TUNEL methods were used to compare the cytology and biochemistry of pleural effusion and cancer cells planted to the surface of pleura before and after therapy. Kang et al. disclose pyknosis and disintegration of nuclei and apoptotic bodies were found by optical and electron microscopy (see Abstract).

10. Mok et al. teach identification of potential serum markers in ovarian cancer using microarray technology. RNA was isolated and pooled from three ovarian cancer cell lines and from three normal human ovarian surface epithelial cells lines.

Complementary DNA generated from these pools was hybridized to a microarray slide and genes overexpressed in the cancer cells were identified (see Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use pleural effusions instead of serum to isolate RNA from apoptotic bodies for the diagnosis of lung carcinoma in a patient. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Kopreski et al. and Kang et al., because Kopreski et al. teach a method of diagnosing cancer in a patient by isolating RNA from apoptotic bodies and Kang et al. disclose a method of analyzing pleural effusions from a lung carcinoma patient and identifying that apoptotic bodies are present in the fluid.

Therefore one of ordinary skill in the art would be motivated to use other bodily fluids,

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that contain apoptotic bodies in the diagnostic method taught by Kopreski et al.

Furthermore, It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the technique taught by Mok et al. to identify RNA of apoptotic bodies in serum/plasma samples. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Kopreski et al. and Mok et al. because the microarray technology would allow a potential screening method to detect increased levels of RNA from apoptotic bodies in bodily fluid samples with a high throughput.

All other rejections of record are withdrawn in view of Applicants amendments to the claims in the reply filed on 07/30/2009.

Conclusion

11. Claims 10-15, 18-20, and 23 are rejected.
12. No Claim is allowed.
13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to MEERA NATARAJAN whose telephone number is (571)270-3058. The examiner can normally be reached on Monday-Thursday, 9:30AM-7:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Larry R. Helms/

Supervisory Patent Examiner, Art Unit 1643